

REMARKS

The Present Invention

The present invention is directed to an adenoviral vector for expressing a heterologous gene in a host cell, a host cell infected with such a vector, a method of producing a selected protein by culturing a host cell infected with such a vector, and a method of delivering a heterologous gene to an animal heart *in vivo* by administering such a vector to the animal heart.

The Pending Claims

Claims 1, 3, 4, 9, and 17-22 are pending. Claims 1, 3, 4, 9, 17, 21, and 22 are directed to an adenoviral vector. Claim 18 is directed to a host cell. Claim 19 is directed to a method of producing a selected protein. Claim 20 is directed to a method of administering a heterologous gene to an animal heart *in vivo*.

The Office Action

The Office Action objects to the Abstract for allegedly being longer than one paragraph and greater than 150 words in length. Claims 1, 9, and 17-19 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schneider et al., *J. Gen. Virol.*, 70, 417-427 (1989) in view of Huang et al., *Nucl. Acid Res.*, 18(4), 937-947 (1990), and Choi et al., *Mol. Cell. Bio.*, 11(6), 3070-3074 (1991). Claims 3, 4, 20, 21, and 22 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of the Schneider, Huang, and Choi references in further view of Fang et al., *Hepatology*, 10, 781-787 (1989), Kaufman et al. (U.S. Patent 4,740,461), Stratford-Perricaudet et al., *J. Clin. Invest.*, 90, 626-630 (1992), and/or Fields (In *Fundamental Virology*, Raven Press, New York, p. 795 (1990)). Reconsideration of these rejections is hereby requested.

Discussion of Objection to Abstract

The abstract has been objected to for being longer than one paragraph and for containing more than 150 words. The amended abstract set forth herein consists of one paragraph and is less than 150 words in length. Thus, the objection to the abstract is rendered moot by the amended abstract.

Discussion of Rejections Under 35 U.S.C. § 103(a)

Claims 1, 9, and 17-19 have been rejected under Section 103(a) as allegedly being unpatentable over the Schneider reference in view of the Huang reference and the Choi reference. Claims 3, 4, 20, 21, and 22 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of the Schneider, Huang, and Choi references in further view of the Fang reference, the Kaufman reference, the Stratford-Perricaudet reference, and/or the Fields reference. These rejections are traversed for the reasons set forth below.

According to the Office Action, the Schneider reference discloses an adenoviral vector comprising a herpes virus TK promoter inserted into a Bam HI site within the E3 region of the adenoviral vector, such that the TK promoter is oriented opposite to the direction of E3 transcription. The adenoviral vector can further contain a heterologous gene under the regulatory control of the TK promoter, as well as a TK polyadenylation site.

The Office Action concedes that this adenoviral vector, with a heterologous gene inserted in the opposite orientation as adenoviral transcription, is not the same as the claimed invention. For example, the adenoviral vector disclosed in the Schneider reference does not contain a eukaryotic splice acceptor and splice donor site positioned downstream of the TK promoter and upstream of the polyadenylation site, as required by the pending claims. The Office Action relies on the Huang, Choi, Fang, Kaufman, Stratford-Perricaudet, and Fields references as allegedly curing the various deficiencies of the Schneider reference vis-à-vis the pending claims.

One of ordinary skill in the art, however, upon reading the Schneider reference, either alone or in combination with the other cited references, would not be led to make or use the invention as presently claimed.

The Schneider reference discusses adenoviral vectors with heterologous genes inserted in both the same orientation and the opposite orientation as adenoviral transcription. In particular, the Schneider reference discloses that the glycoprotein gene of vesicular stomatitis virus (VSV) operatively linked to a TK promoter and HSV polyadenylation site was inserted into the E3 region in both transcriptional orientations. The Schneider reference reports that detectable production of the VSV glycoprotein *only* was obtained from the adenoviral vector having the TK-VSV insert in the *same orientation* as E3 transcription (see, e.g., Abstract, and page 420, second complete paragraph). While the TK promoter was found to be functional in both orientations, only a minimal amount of VSV transcripts were produced when the TK promoter was oriented opposite to E3 transcription, as compared to the high level of VSV transcription that occurred when the TK promoter was oriented in the

same transcriptional orientation as the E3 region. According to the authors, these results suggest difficulty in transcribing through the E3 region from right to left when high levels of adenoviral transcription are occurring from left to right (see, e.g., page 422, second complete paragraph).

In view of the reported high level of VSV transcription achieved when the VSV glycoprotein expression cassette was oriented in the same direction as adenoviral E3 transcription, one of ordinary skill in the art considering the Schneider reference would be led to construct an adenoviral vector with a heterologous gene inserted in the *same transcriptional orientation* as the E3 region. Thus, to the extent that one of ordinary skill in the art would have combined the disclosures of the other cited references with the disclosure of the Schneider reference to provide a new adenoviral vector, the resulting new adenoviral vector would have been an adenoviral vector with a heterologous gene inserted in the *same orientation* as adenoviral transcription – *not* in the *opposite orientation* as adenoviral transcription as required by the pending claims. In other words, by actually following the teachings of the cited references (assuming *arguendo* that the cited references properly are considered together), one of ordinary skill in the art would not have been led to the present invention, but rather would have been led away from the present invention.

The fact that one of ordinary skill in the art would have been led away from the claimed invention by the disclosures of the cited references is important in considering the possible obviousness of the present invention. An allegation of obviousness can be rebutted if the prior art is shown to “teach away” from the claimed invention. A reference may be said to teach away “when a person of ordinary skill, upon reading the reference ... would be led in a direction divergent from the path that was taken by the applicant.” See, e.g., *In re Haruna*, 249 F.3d. 1327, 58 U.S.P.Q.2d. 1517 (Fed. Cir. 2001), and M.P.E.P. § 1504.03.

In view of the teachings of the Schneider reference, the cited references provide no motivation for constructing an adenoviral vector as presently claimed. Indeed, one of ordinary skill in the art would have been motivated to prepare an adenoviral vector quite different from the adenoviral vector as defined by the pending claims. Since the cited references, considered together, teach away from the invention defined by the pending claims, the present invention must be considered to be patentable in view of the cited references, and the Section 103(a) rejections should be withdrawn.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the

In re Appln. of Falck-Pedersen
Application No. 08/653,114

Examiner, a telephone conference would expedite the prosecution of the subject application,
the Examiner is invited to call the undersigned agent.

Respectfully submitted,



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